SOME ASPECTS OF THE ETIOLOGY OF LEUKEMIA IN PRIMATES, INCLUDING MAN

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The virus etiology of the overwhelming majority of leukemias in animals is no longer disputed. Meanwhile the possibility of virus etiology of leukemias in man and other representatives of the Primate Order continues to provoke discussion. One probable agent of some forms of human lymphomas is Epstein-Barr virus (EBV), which is being studied extensively in many countries.

To study the possible viral nature of human leukemias, we injected blood from human leukemia patients into monkeys of various species (brown macaques — *Macaca aretoides*; Abyssinian baboons — *Papio hamadryas*), as a result of which some of the animals developed hemoblastosis after a varied time interval [1, 3].

DNA- and RNA-containing viruses were isolated from the sick monkeys, and one of them — lymphotropic baboon herpes virus (BHV) was found to be closely related (but not identical) to EBV.

A careful study of this virus (immunologic, molecular-biological, and morphologic), and a study of its biology and associated pathology led to formulation of the concept, which has been confirmed more recently, that there exists a family of EBV-like lymphotropic oncogenic herpes viruses of primates (baboons, chimpanzees, gorillas, orangutans, and green guenons) [2, 5, 7, 13]. BHV virus has transforming activity for lymphocytes of several species of monkeys and man and induces a fatal lymphoproliferative disease in South American monkeys [6].

Virus hemoblastosis of baboons and macaques has successfully undergone passage in animals of these same species. A horizontal spread of the disease also has been observed following close contact between sick and healthy animals. By now, as a result of inoculations and contact between sick and healthy animals, 218 members of a herd of Abyssinian baboons have died from various forms of hemoblastosis in the period since 1967 (this is about 7% of the total number of animals). Of 258 brown macaques, in which 20 successive passages have been carried out after inoculation with blood from patients with leukemia, 2% have died from generalized malignant lymphoma [2].

Besides lymphotropic herpes virus, which has appeared in the literature under the abbreviation BHV†, endogenous baboon viruses also have been isolated from leukemia Abyssinian baboons: xenotropic — BILN [8], and ecotropic — EPHV‡ [2], the role of which in the pathogenesis of hemoblastosis has not yet been explained.

One of the viruses, which because of the site of its discovery we call plasma, and which was present in the blood of baboons and macaques with lymphoma, differed immunologically from all known animal oncoviruses [2, 4].

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†Direct transliteration from the Russian would be GVP.
‡Direct transliteration from the Russian would be EVPG.

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TABLE 1. Frequency of Discovery of Antibodies against HTLV in Blood of Abyssinian Baboons and Brown Macaques

Source of sera	Number of animals tested	Number of positive reactions	
		absolute	%
Abyssinian baboons with hemoblastosis	38	38	100
Clinically healthy Abyssinian baboons: at increased risk	13	13	100
Forest herd with low-density contact	35	2	6
With no contact	33*	0	0
Brown macaques innoculated primarily with blood from human leukemia patients and in passages	7	1 †	14

Legend. *Sera taken on day of arrival of monkeys from Ethiopia, †immunofluorescence reaction was ± in two other macaques of this group.

TABLE 2. Results of Investigation of Sera of Healthy Asiatic Monkeys for Antibodies against HTLV

Species of monkey	Number of animals tested	Number of positive reactions	
		absolute	%
Rhesus monkeys (M. mulatta)	8	0	0
Pig-tailed macaque (M. nemestrina)	12	0	0
Long-tailed macaque (M. fascicularis)	11	0	0
Chimpanzee (Pan troglodites)	8	0	0

In 1981, a high frequency of T-cell leukemias was found in Japan, mainly in the coastal region of Kyushu Province. A C-type oncovirus, subsequently named HTLV/ATLV, was isolated from the affected persons [10, 12, 14]. High titers of antibodies against the virus were found in the blood of the affected patients and also of persons in close contact with them. This virus is now regarded by research workers as the first oncovirus of human leukemia. Meanwhile reports have been published to indicate the presence of a virus similar to HTLV in Japanese macaques (*M. fuscata*), and also in African green guenons [11, 15].

These investigations, and also the presence of T-cell lymphomas in Abyssinian baboons, led us to study the sera of these baboons and brown macaques with lymphomas, baboons from a herd at increased risk of developing lymphoma, and also two control groups of baboons. The latter differed from each other in that the monkeys of one group had been in contact with a monkey (male) from the group at increased risk (a forest herd), whereas the second group was composed of monkeys recently arrived from Ethiopia.

The investigation was carried out by an immunofluorescence method. Cells of strain NIT-102, producing HTLV virus, were used as the antigen (the strain was generously provided by Dr. A. D. Al'shtein).

The results of investigation of the sera from baboons and macaques with lymphoma, and also from control animals, are given in Table 1. Antibodies against HTLV antigen were found in all baboons with malignant lymphoma and also in all healthy animals of the herd at

increased risk of developing malignant lymphoma, unlike in the healthy control baboons with no contact with monkeys affected by lymphoma (the group tested on the first day after their arrival from Ethiopia). In the case of low-density contact (forest herd) antibodies against HTLV were found in only individual monkeys.

Among the small group of macaques tested in experiments to study inoculation with hemoblastosis, antibodies against HTLV also were found in some animals (Table 1).

Investigation of sera from control Asiatic monkeys (31 macaques) and also eight sera from healthy chimpanzees which were in our possession, revealed no antibodies against HTLV (Table 2).

The investigation of sera of 126 monkeys (baboons and macaques) inoculated with leukemic material or developing malignant lymphoma as a result of contact, and also of control animals, thus revealed that all monkeys with lymphoma and also all animals from a herd at increased risk, i.e., in contact with sick animals or inoculated with leukemic material, were seropositive for HTLV. The possibility of infection with the virus depended on the density of contact (forest herd).

The following hypotheses can be put forward on the basis of the facts described above: 1) the species of monkeys belonging to the Sukhumi herd became seropositive as a result of inoculation with human leukemic material containing HTLV, and subsequent horizontal spread of this virus within the herd; 2) monkeys and man can be infected by the same C-type oncoviruses which plays a possible etiologic role in the development of hemoblastosis in various representatives of the Primate Order.

A final conclusion on this issue can be drawn only after isolation and thorough immunologic and molecular-biological investigation.

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